Conventional Brachytherapy In Carcinoma Cervix.
A HISTORICAL PERSPECTIVE

Dr. RAKESH KAPOOR
MD, MAMS, FICRO
Professor & Head Unit II
Department of Radiotherapy and clinical Oncology, Tertiary Cancer Center, PGIMER
Chairman Indian College Of Radiation Oncology.
Founder Director HBCH & RC Punjab. (Unit of T.M.C, Mumbai) DAE,(GOI)
Ex. Head: Department of Biostatistics, P.G.I.M.E.R
Ex. Additional Medical Superintendent, P.G.I.M.E.R

BRACHYTHERAPY

- Brachy
  Short distance (Greek)
- Brachytherapy is a type of radiation treatment in which small, encapsulated radioactive sources are arranged in a geometric fashion in & around tumor.
- ADV.
  - *It delivers very high dose of radiation to tumor*
  - *Sparing normal tissue*
  - *Dose delivered in short duration as compared to External beam RT.*
- Cavity
  Hollow space within the body.
  Lumen – cavity within a tubular organ.
- Intracavitary brachytherapy
  Gynecological sites – cervix, uterus, vagina.

Anatomy & Pathology

- ***Relationship of uterus & vagina***
  - Uterus is usually anteverted & anteflexed and it lies at right angles to the vagina.
    - Construction of applicator.
- ***Relationship of rectum & bladder***
  - Important consideration regarding the dose received by brachytherapy – complications
- ***Spread of disease***
  - Predominant line of spread – laterally thru paracervical tissues into parametrium
  - Into uterus & vagina
  - Only in very advanced – into bladder & rectum
  - Brachytherapy doses should reach more laterally than anteroposteriorly

Types of IC brachytherapy

- **Depending upon loading technology**
  - Preloaded – radium tubes
  - After loaded
    - Manual – Cs^{137}
    - Remote – Cs^{137}, Co^{60}, Ir^{192}.
- **Based on dose rates used**
  - Low dose rate – LDR
    - 0.4-2 Gy/ hr
    - Ra^{226}, Cs^{137}
  - Medium dose rate – MDR
    - 2-12 Gy/hr
    - Cs^{137}
    - In PGI we consider, any dose rate > 0.9 Gy/hr which require dose rate correction as MDR.
  - High dose rate – HDR
    - > 12 Gy/hr
    - Co^{60}, Ir^{192}

WHY I/C BRACHYTHERAPY

- Optimal conformal dose delivery system.
- Inhomogeneous dose – very high dose locally, rapid fall off.
    - Cervix receives 20,000 – 25000 cGys.
    - Uterus receives 20,000- 30000 cGys.
    - Vagina receives 10,000 cGys.

  such high doses can’t be delivered by any technique of EBRT.
- Sparing of early & late responding normal tissues.
- Short overall treatment time
- Counter tumor repopulation.
- Best long-term control is achieved
- Less late radiation morbidity .
- Preservation of normal anatomy.
- Better sexual functional life.

BRACHYTHERAPY in Cervix

- Brachytherapy plays vital role in treatment of ca cx. & is mainly applied as an intracavitary procedure in selected cases complemented by interstitial implants.
- **Cervical cancer** is an ideal site for I/C brachytherapy because
  - High tolerance of cervix ,uterus & vagina
  - It is accessible organ hence Brachytherapy can be practiced with ease.
  - The endocervical canal & vaginal vault form a suitable vehicle to carry rigid applicators with radioactive sources.
  - These applicators can be used with minor modifications in all pts.
- I/C applications are temporary that are left in the patient for a specified time to deliver prescribed dose.

HISTORY

1898 : Discovery of Radium by Marie Curie in Paris.

1903: Margaret Cleaves, a New York physician described inserting Radium into the Uterine cavity of a patient with Ca Cervix.

1908 : I/C brachytherapy started in Vienna

1910: I/C brachytherapy started in Stockholm

1912: I/C brachytherapy started at Paris.

1930: Todd & Meredith developed Manchester system in U.K.

1960s: After loading technique (Helneski)

1970: Paris System of dosimetry for Interstitial Brachytherapy evolved

1975: Remote Control LDR (Cs-137)

1985: -HDR Introduces(Ir-192 & Co-60) & ICRU-38 Published

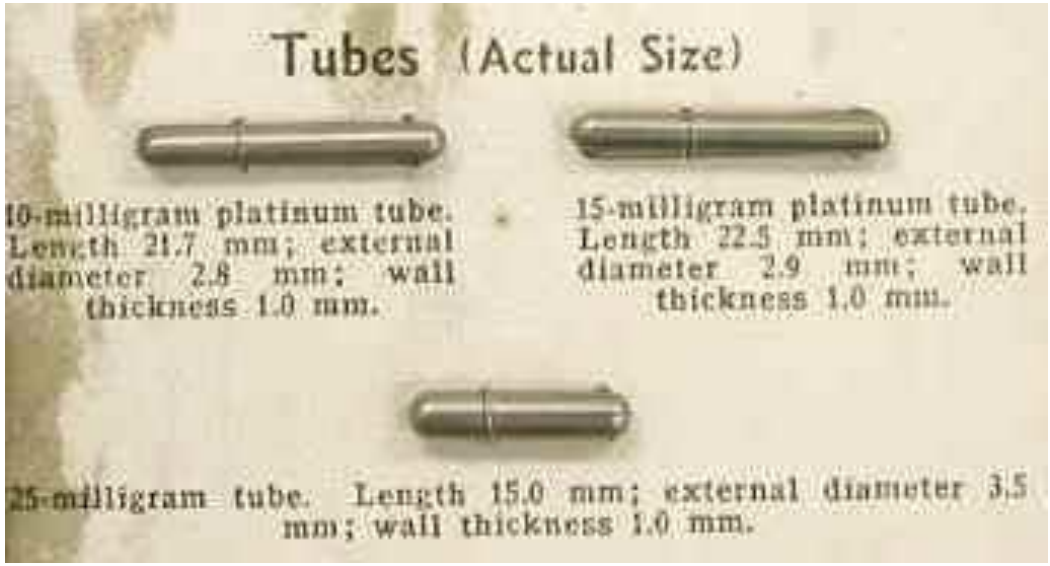
-Concept of Volume in place of point introduced

-Joshlin Published data about the discrepancies in point A & B

1990s: Miniaturized stepping source with optimization

SOURCES

- Radium 226 - LDR
  - As tubes, with 1 mm platinum filtration.
  - Avg energy – 0.83 MeV
  - Half life – 1626 yrs.
- Cobalt 60 - HDR
  - High dose rate system
    - Pellets similar to Cs137.
    - Higher activity – 500 mCi/pellet
- Iridium 192 - HDR
  - Active wire – (dia -0.2-1.3 mm, AL – 1-20 mm)
    - Nucletron – 1.1 mm, 4 mm
  - Encased in stainless steel
  - Permanently attached to cable drive.
  - Activity – 10 Ci (370 GBq)



Radium 226

- Cesium 137 - LDR/MDR
  - Manual after loading.
    - Miniature cylindrical sealed sources – 5x1.8 mm.
    - Active bead – 1.1 mm diameter
    - Spherical steel spacers – 1.8 mm
  - Remote after loading
    - Incorporated into glass bead – 1.5 mm diameter
    - Encapsulated – stainless steel ball bearing – 2.5 mm diameter.
    - Activity – 40 mCi/pellet
  - Preloaded
    - In forms of tubes, similar to radium
    - 25 mg – (TL-2 cm, AL-1.35 cm, Dia- 4.05 mm)
    - 20 mg – (same dimensions)

DOSIMETRIC SYSTEMS

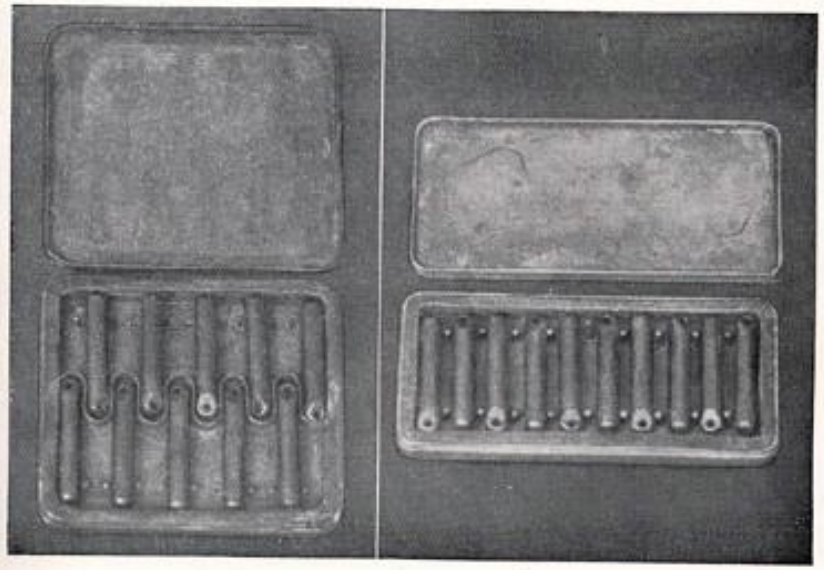
- The historical dosimetric systems were developed when computer treatment planning and dose computations were not available

- Term ‘system’ specifies a set of rules for
  - Geometrical arrangement of a specific set of radio isotopes in a specialized applicator
  - To obtain suitable dose distributions over the volume to be treated.
  - It specifies treatment in terms of the dose, time and administration
  - A specified set of tables to allow, reproducible and easy calculation in most of the encountered clinical scenarios.
  - A system ensures safety and is based on clinical experience.

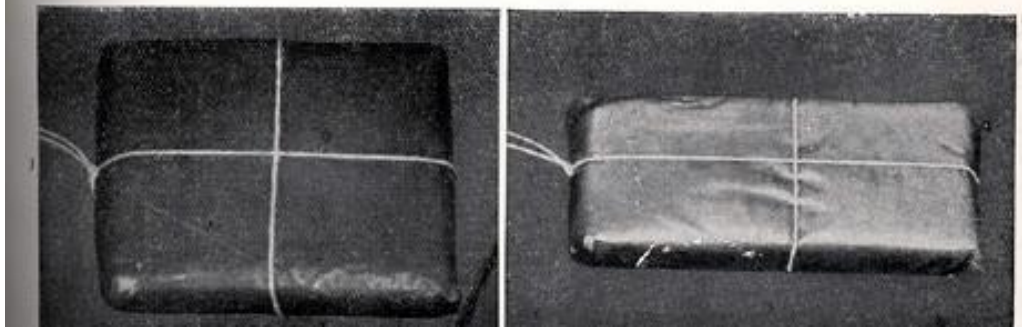
STOCKHOLM SYSTEM

- Work of Forsell at radium hemmet -1910
  - Unequal amounts of radium used.
    - Uterus – 30-90 mg in rigid tube
    - Vagina – 60-80 mg in shielded lead/silver boxes
    - Vaginal & uterine applicators – not fixed
- Fractionated (2-3 #s) course over a period of one month.
- Heavy doses for a period of 20-30 hours each.
- Separated by 1-3wks
- This system used
  - Intravaginal boxes made up of silver or gold
  - The intrauterine tube made up of flexible rubber.
  - These were not fixed together

Figs. 7 and 8. Flat applicators of various types for vaginal application. Full size. The property of Radiumhemmet.



Figs. 9 and 10. The same applicators with their tubes.



- Unequal amounts of radium used.
  - •Uterus – 30-90mg in rigid tube
  - •Vagina – 60-80mg in shielded lead/silver boxes
  - •Vaginal & uterine applicators –not fixed

  - •Heavy doses, each lasting 20-30hrs
  - •6500 – 7100 mg hrs.

  - •Results -1914-25 (5 yr results)
  - •Treated -1455
  - •Symptom free -327
  - •Cure rate – 22.5%
- A total dose of 6500 -7100 mg -hrs was prescribed out of which 4500 mg Ra was contributed by the vaginal box. (dose rate-110R/hr)

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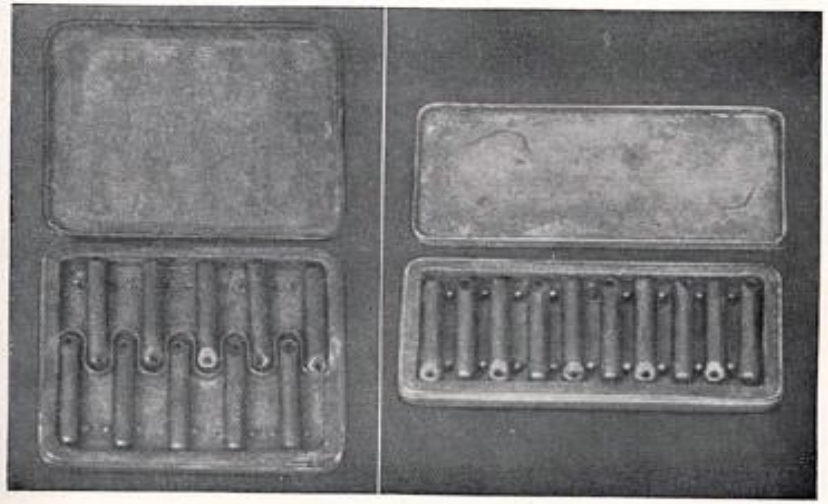

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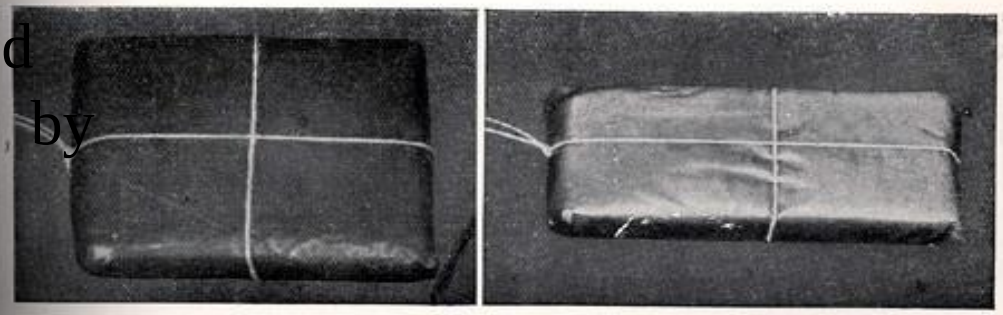
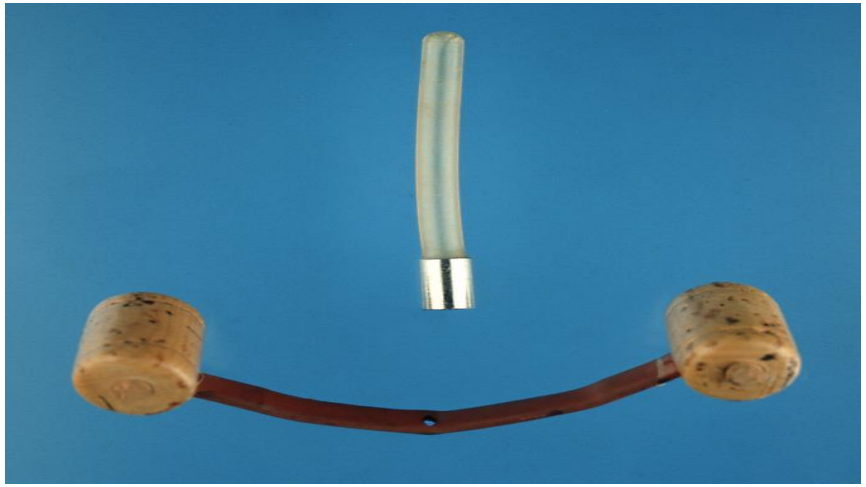
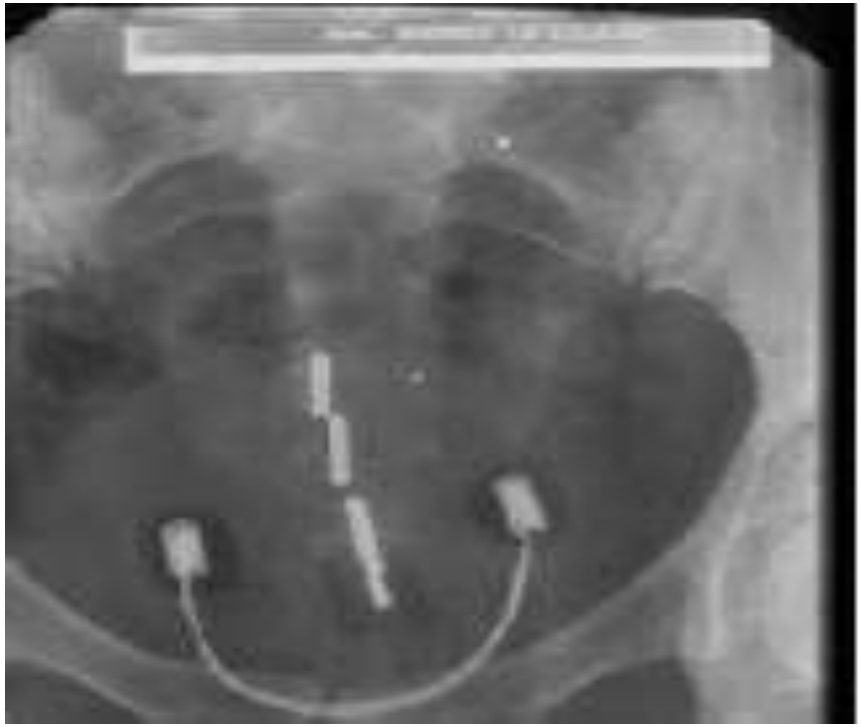


Figs. 11 and 12. The same applicators ready to be introduced into the vagina.

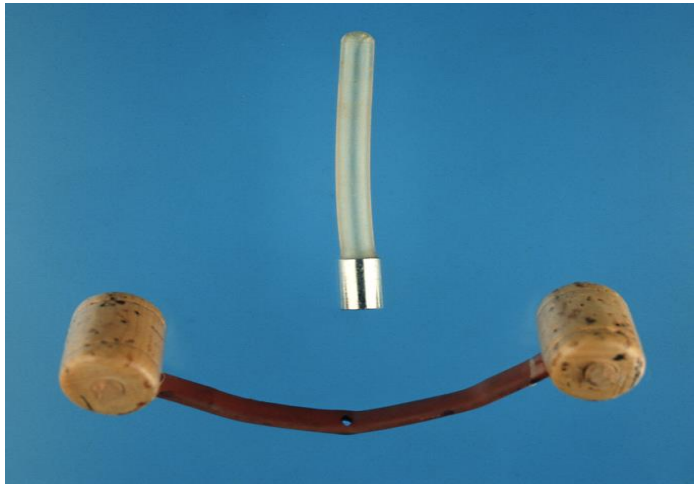
PARIS SYSTEM

- Regaud, 1919, Institute of radium, Paris
- Single application of Radium for 120 hrs (5-6days)
- Designed to deliver a dose of 7000 - 8000 mg/hrs over a period of 5 days (45 R/hr) (5500 mg/hr)
- In this system, almost an equal amount of Radium was used in the uterus and the vagina.
- The system incorporated
  - Two cork colpostats (cylinder) with 13.3mg Radium in each
  - An intrauterine tube of silk rubber with 33.3mg Radium
- The intrauterine sources contained three radioactive sources, with source strengths in the ratio of 1:1:0.5





- Regaud, 1919, Institute of radium, Paris
- Fixed mg-hrs for a specified tumor volume.
- Smaller amounts of radium for longer time.
- Uterus – 6.6+13.33+13.33 mg Ra – rubber tubes
- Vagina - 13.33 in each cork colpostats.
- Time: 120 hrs
- 7200-8000 mg hrs.
- Initially colpostats alone → colpostats+ tandem → tandem alone.
- Results – 1923
    - Symptom free survival -43.9%



Designed to deliver a dose of 7000 - 8000 mg hrs over a period of 5days (45R/hr) (5500mg/hr)

FALLACIES

- Long treatment time, discomfort to the patient
- Dose prescription method was empirical. Both systems specified dose in mg-hour.
- Does not give any information about dose distribution.
- When used in conjunction with EBRT, overall radiation treatment can’t be adequately defined
- Dose specification method lacks the information on
  - Source arrangement
  - Position of tandem relative to the ovoids
  - Packing of the applicators
  - Tumour size, and
  - Patient anatomy.
- With the use of this dose prescription method dose to important anatomical targets could not be quantified adequately.
- Ignored the importance of tolerance of different critical organs to radiation.

DOSE SPECIFICATION

- Done in mg-hr i.e. simple mathematical product of mg of Radium times the duration (in hours) of the implant.
- It was easy to use.
- The dose prescription was entirely empirical due to the lack of
  - knowledge about the biological effects of radiation on the normal tissues and the tumor
  - understanding about the dose, dose distribution and the duration of treatment.
- Only applicable when both tandem & ovoids are used & sources are loaded in a rigidly prescribed manner.

MANCHESTER SYSTEM

- The Manchester system is one of the oldest & extensively used systems in the world.
- Developed by Todd & Meredith in 1930 & was in clinical use by 1932.
- This system was initially developed for radium tubes but was easily adapted to different afterloading systems.
- Predetermined doses & dose rates to reduce the empirism & high complication rates.
- Dose specified at fixed points – point A
- Specified therapy in terms of absorbed dose – Roentgen instead of mg hrs.
- Initially preloaded → manual after loaded → remote after loaded.
- Initially for LDR. Now used for MDR & HDR also.

Manchester system was based on following principles:

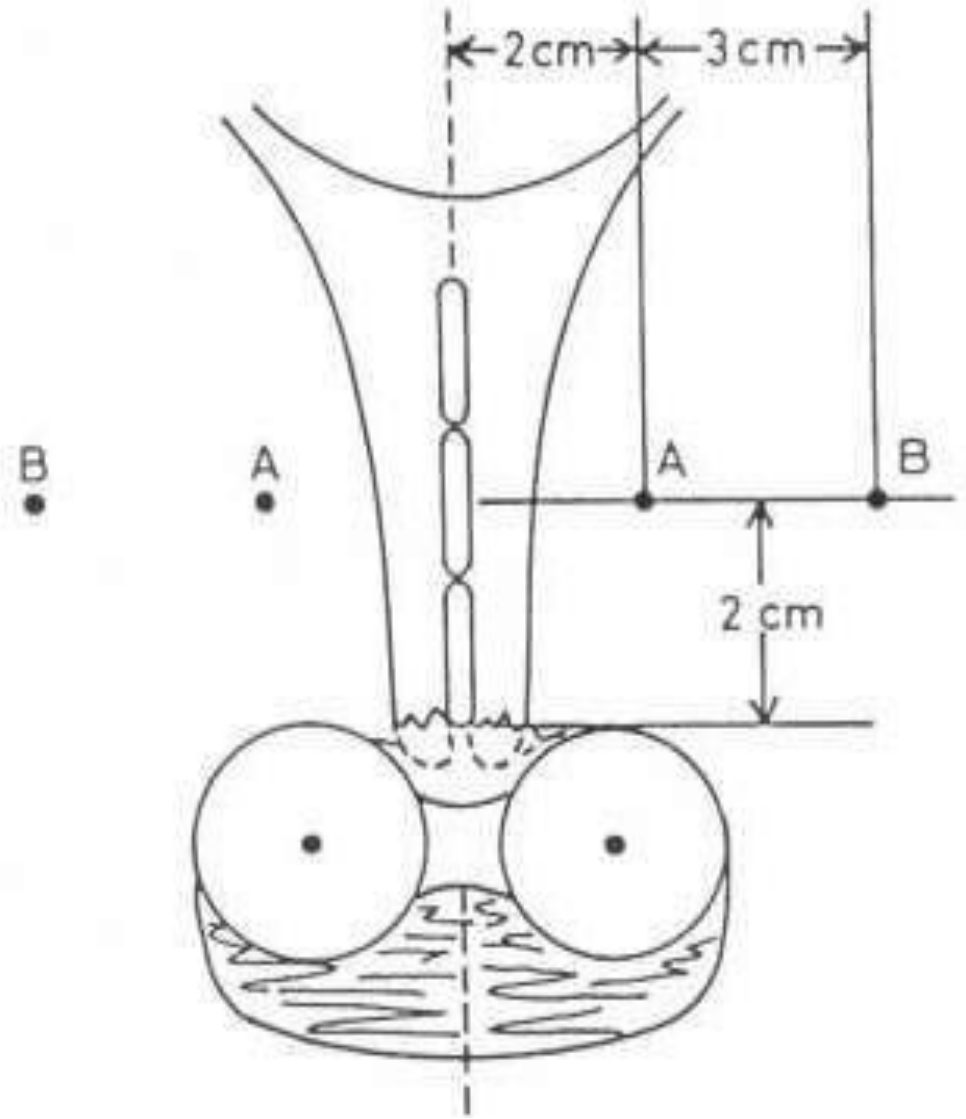
- To define the treatment in terms of dose to a point
  - It should be anatomically comparable from patient to patient.
  - Should be in a region where the dosage is not highly sensitive to small alteration in applicator position.
  - Should be in position that allows correlation of dose with clinical effects

- To design a set of applicators and their loading (with a given amount of radium), which would give the same dose rate irrespective of the combination of applicators used.

- To formulate a set of rules regarding the activity, relationship & positioning of the radium sources in the tandem & vaginal ovoids to achieve desired dose rate.

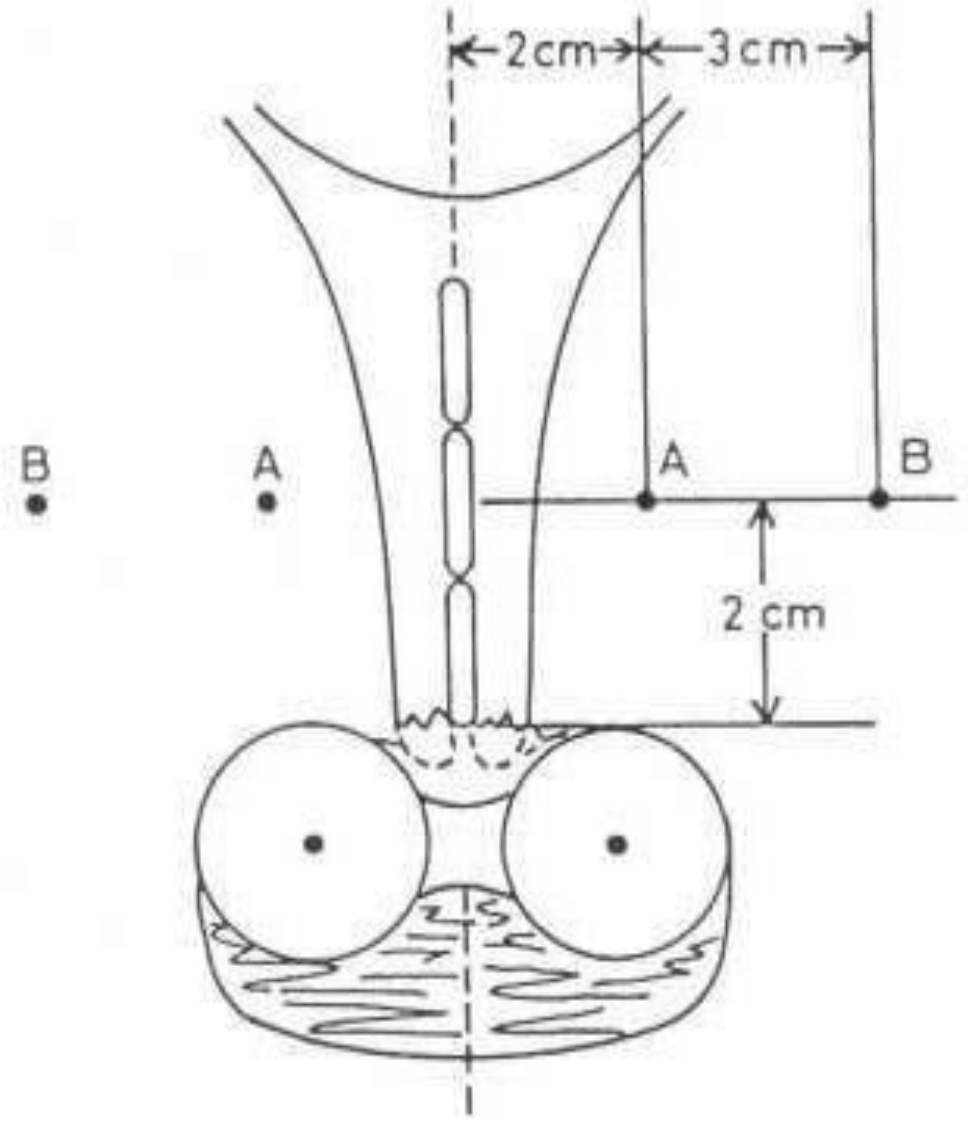
POINT A

- Todd & Meredith defined a point in paracervical triangle where the uterine vessels cross the ureter as point A.
- Point A, lies in the paracervical triangle.
- Point A is defined as a point 2 cm. lateral to the center of the uterine canal and 2 cm. superior to the mucosa of the lateral fornix, in the plane of the uterus.
- Now point A is defined as a point 2 cm above the distal end of lowest source in cervical canal & 2 cm lateral to centre of tandem.
- ABS recommends this point as it falls within the portion of the isodose distribution with little cephalocaudal gradient.



POINT B

- To know the rate of fall of dose external to point A, as an index to the volume of tissue treated.
- Quantifies the dose delivered to the obturator lymph nodes.
- Point B is defined 2cm above external os & 5 cm laterally to midline.
- Represents dose to the pelvic wall, obturator L.N.
- The dose at point B is approx. 25 -30% of the dose at point A.
- Dose to point B, depends little on the geometric distribution of radium, but on the total amount of radium used.



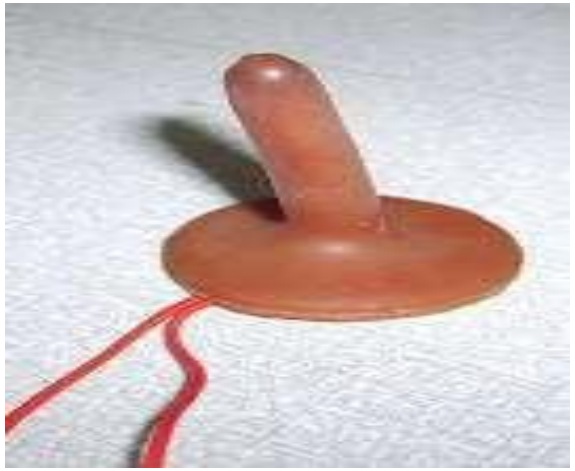
DOSE LIMITING STRUCTURES

- Bladder
- Rectum
- Vaginal mucosa
- Rectovaginal septum
  - No more than 40% of total dose at point A could be delivered safely through the vaginal mucosa.
  - The rectal dose should be 80% or less of the dose at point A; this rectal dose can usually be achieved by careful packing.

APPICATOR IN MANCHESTER SYSTEM

- Similar to those used in Paris system
- It had a pair of ovoids & an intrauterine tube
    - Intrauterine applicator
        - Rubber tubing, with flange at end.
        - Varying length, can take – 1,2,3 radium tubes in line.
    - Ovoids
        - Rubber or nylon
        - Shape follows the distribution in 3-D space of the isodose curves around the contained radium tube, ensuring homogenous dose on its surface.

INTRAUTERINE TUBE



- The intrauterine tube was made up of the thin rubber (to prevent excessive dilatation of the cervical canal)
- These tubes were available in three separate lengths
  - 2cm
  - 4cm
  - 6cm
- In order to accommodate 1, 2 or three Radium tubes (2 cm long) in line I.U.tubes were closed at one end, and had a flange at the other end so that when packed into position, the uterine tube did not slip out during the treatment.

OVOIDS

- Used in pairs, one in each lateral fornix
- The shape of ovoids mimics the shape of isodose curves around a Radium tube having "active length" of 1.5 cm.
- The ovoids were designed to be adaptable to the different vaginal capacity, with diameter of 3 sizes
    - Small – dia = 2 cm
    - Medium – dia = 2.5 cm
    - Large – dia –=3 cm.
- *"WASHER"* – holds the ovoids in position in narrow vagina.
- The largest ovoid are placed in the roomiest vagina in order to achieve the best lateral dose throw off

SPACERS

- Apart from ovoids & I.U.tubes spacers or washers were used
  - To maintain the distance between the ovoids
  - To help in their fixation
- Pairs of ovoids held apart by a "*SPACER"* – rubber.
  - Fixes at a distance of 1 cm.
- Spacer was used to give the largest possible separation b/w the ovoids so that the dose could be carried out as far laterally as possible.
- It maintained a distance of 1cm b/w the ovoids.

PACKING

- Manchester applicators do not incorporate rectal shielding.
- Hence gauze is packed firmly and carefully
  - behind the ovoids,
  - anteriorly b/w the ovoids and the base of the bladder,
  - and around the applicator tubes down to the level of the introitus
- Packing helps to
  - keep the applicators in position
  - to reduce dose to bladder and anterior rectal wall.

RULES

- The point A should receive the same dose rate, irrespective of the combination of applicators used.
- Not more than one third of the total dose to point A should be delivered by the vaginal ovoids. So that tolerance of vagina mucosa is not exceeded.
- Standard or ideal loading is 60-40 i.e. 60% of the dose to point A is contributed by intrauterine sources while 40% is contributed by ovoids.
- Total Dose to point A : 8000 R
  - Total number of applications : 2
  - Total time for each application : 72 hrs
  - Total time : 144 hrs
  - Dose rate desired : 55.5 R /hour to point A
- Amount of radium to be used was defined in terms of units.
- 1 unit = 2.5 mg of radium filtered by 1 mm platinum.
- The loadings were specified in terms of integral multiples of this unit.

LOADING PATTERN

- Total dose at point A using different combinations of IU tube & ovoids :
  - Large tube with large ovoid and washer : 57.5 R
  - Large tube with large ovoid and spacer: 56.9 R
  - Large tube with small ovoid and washer: 57.6 R
  - Medium tube with small ovoids and spacer: 57.3 R

- The variations were thus within 1.5% range.

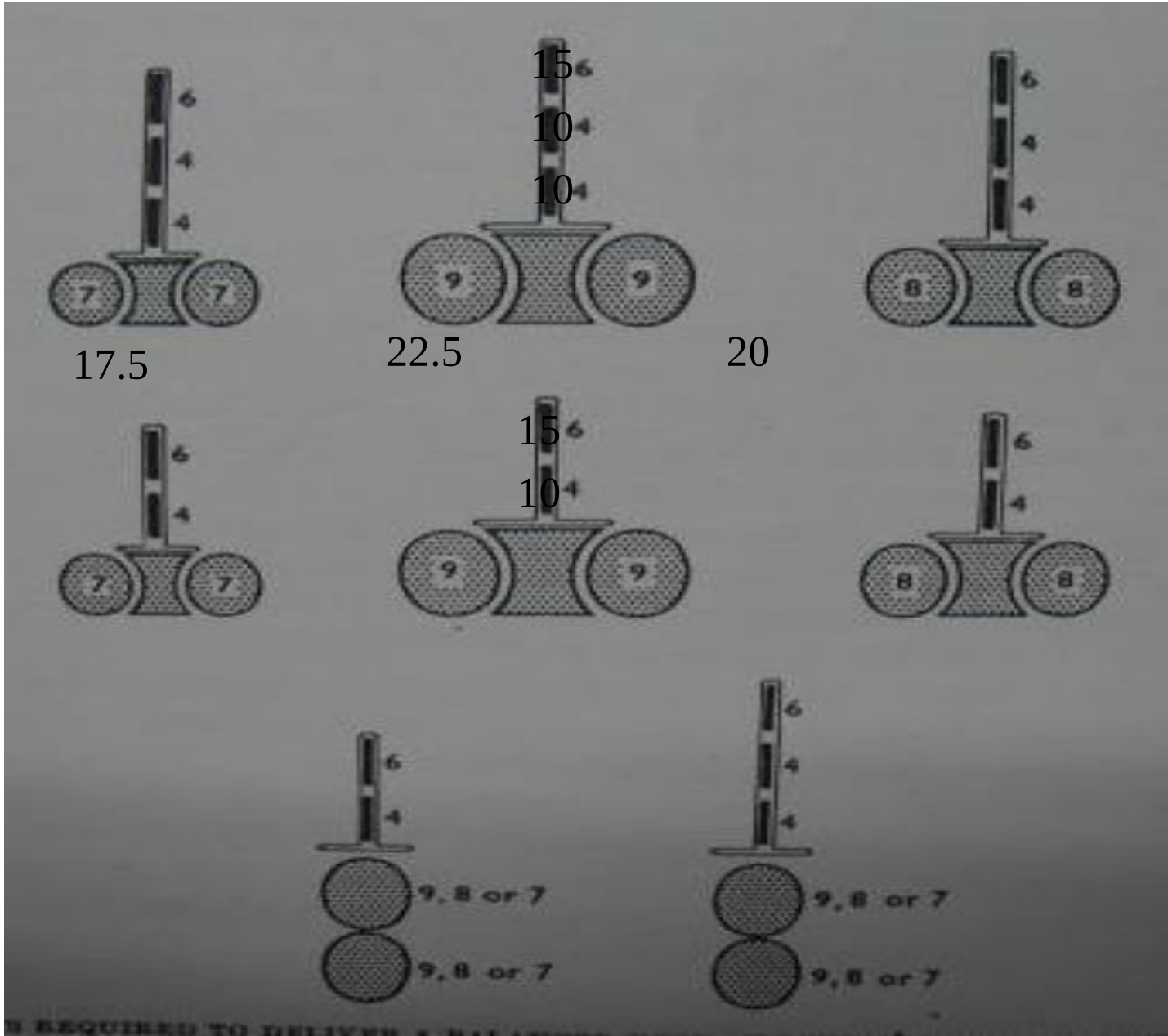
Loading pattern

1 unit = 2.0/2.5/3.33mg

Unit	dose A	dose B
2mg	1000r	large – 39%
2.5	1366r	medium – 33%
3.33	1820r	small – 29%

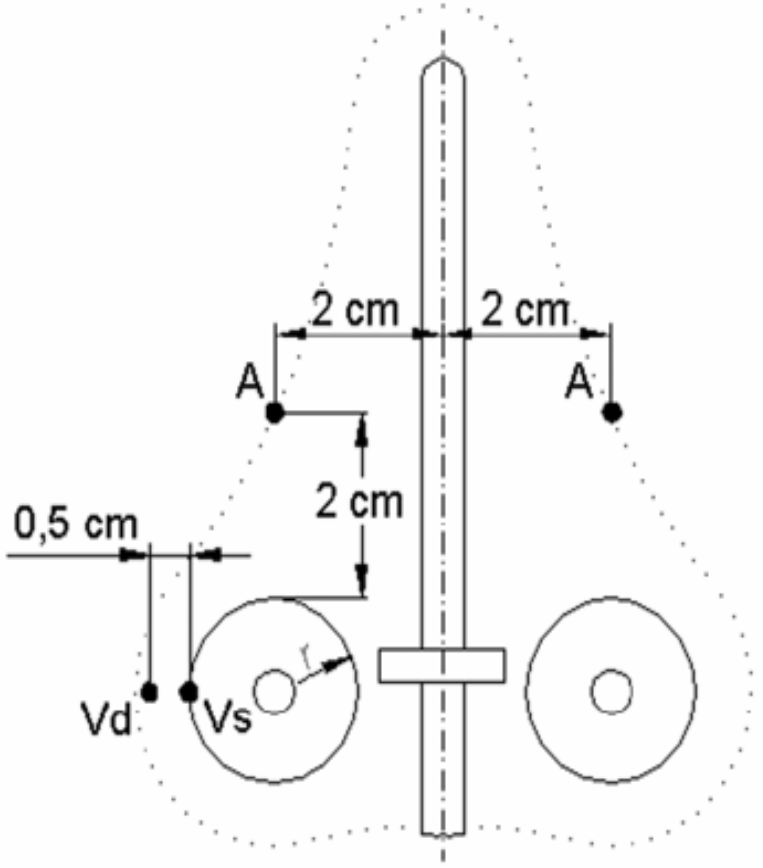
Per 24 hrs.

Using 2.5 mg



Loading pattern

- Vaginal contribution to point A - 40% only.
- Point B dose ~ 9 Gy for every 4000 mg hr.
- Depending upon loading, could deliver from 8400 – 11200 mg hr.
- Dose prescribed – 8000r (72.8Gy) to point A in 2 applications.
  - 70 hrs if 2.5 mg unit.



- Preloaded LDR system.
  - Flexible, loose system- can be inserted even if cervix distorted.
  - Cheap and durable
  - Good geometry attained in experienced hands.
  - Decades of experience
  - Not fixed, high chance of improper geometry, slippage of application.
  - Radiation hazard.
- Preloaded LDR system
  - cesium 137 tubes
- Manual after loaded system
  - Cesium 137, Cobalt 60
    - Reduced radiation hazard.
    - Better application possible.
    - Retains application in position better.

- Remote after loading system.
    - Initially sources as tubes – unpopular –mechanical problems
    - Sources as pellets – 1975 – nucletron.
- Classical LDR – 53cGy/hr
- Modern system – 140 -180 cGy/hr
    - Initially dose rate correction factor not applied.
    - Higher complication rates.
    - Fowler etal -

	75cGy/hr	150cGy/hr
grade 2&3	12%	32%
grade 3	4%	22%

Inspite of 20 % reduction of dose.

ICRU SYSTEM

- For reliable and relevant comparison of different methods and their clinical results ICRU 38 recommends a common terminology for prescribing recording and reporting I/C Brachytherapy applications.
- The ICRU recommends a system of dose specification that relates the dose distribution to the target volume, instead of the dose to a specific point
- The dose is prescribed as the value of an isodose surface that just surrounds the target volume.
- ICRU Reporting
  - Description of technique
  - Dose at reference points
  - Description of reference volume

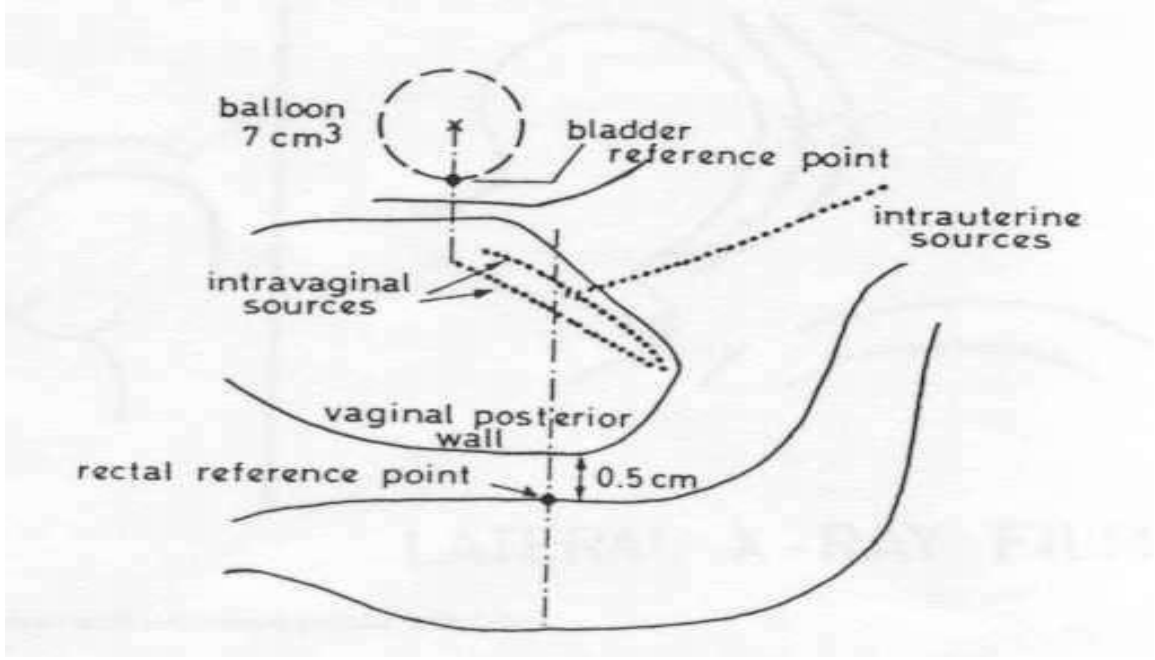
Description of the Technique

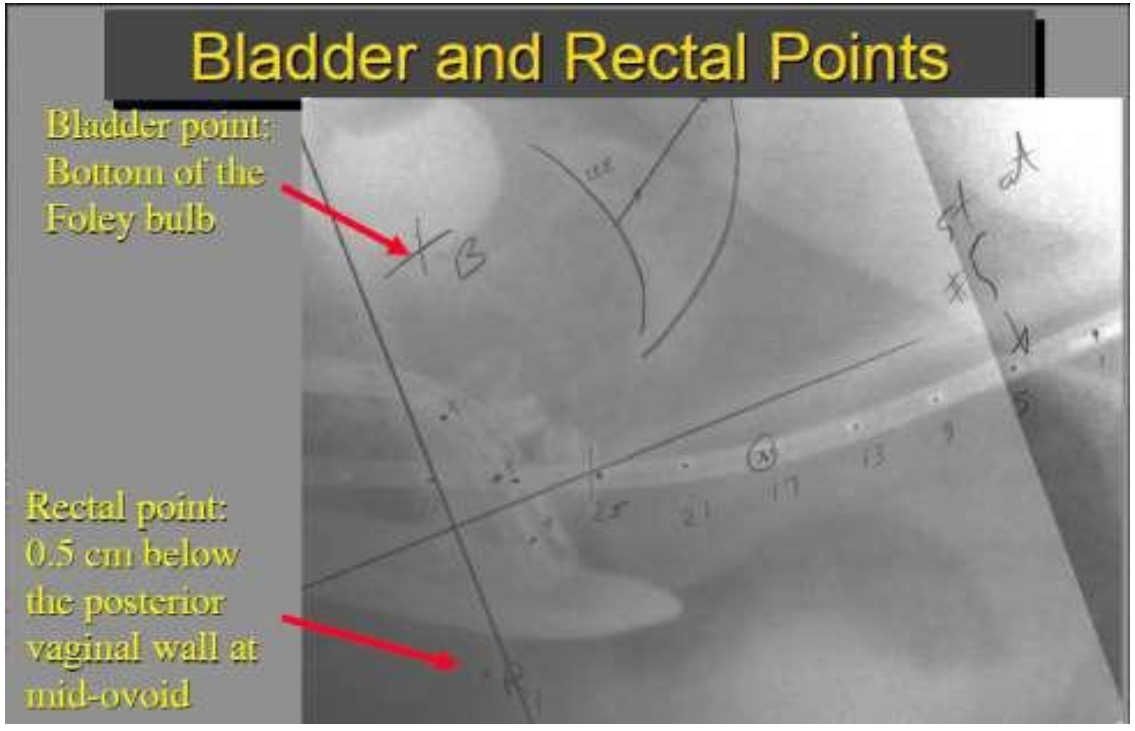
- Minimum information should include the
  - orthogonal radiographs of the application.
  - Source used (radionuclide, shape and size of source, and filtration)
  - applicator type
  - Loading pattern
  - Simulation of linear source for point or moving sources
  - Applicator geometry (rigidity, tandem curvature, vaginal uterine connection, source geometry, shielding material)

Dose at Reference points

BLADDER POINT

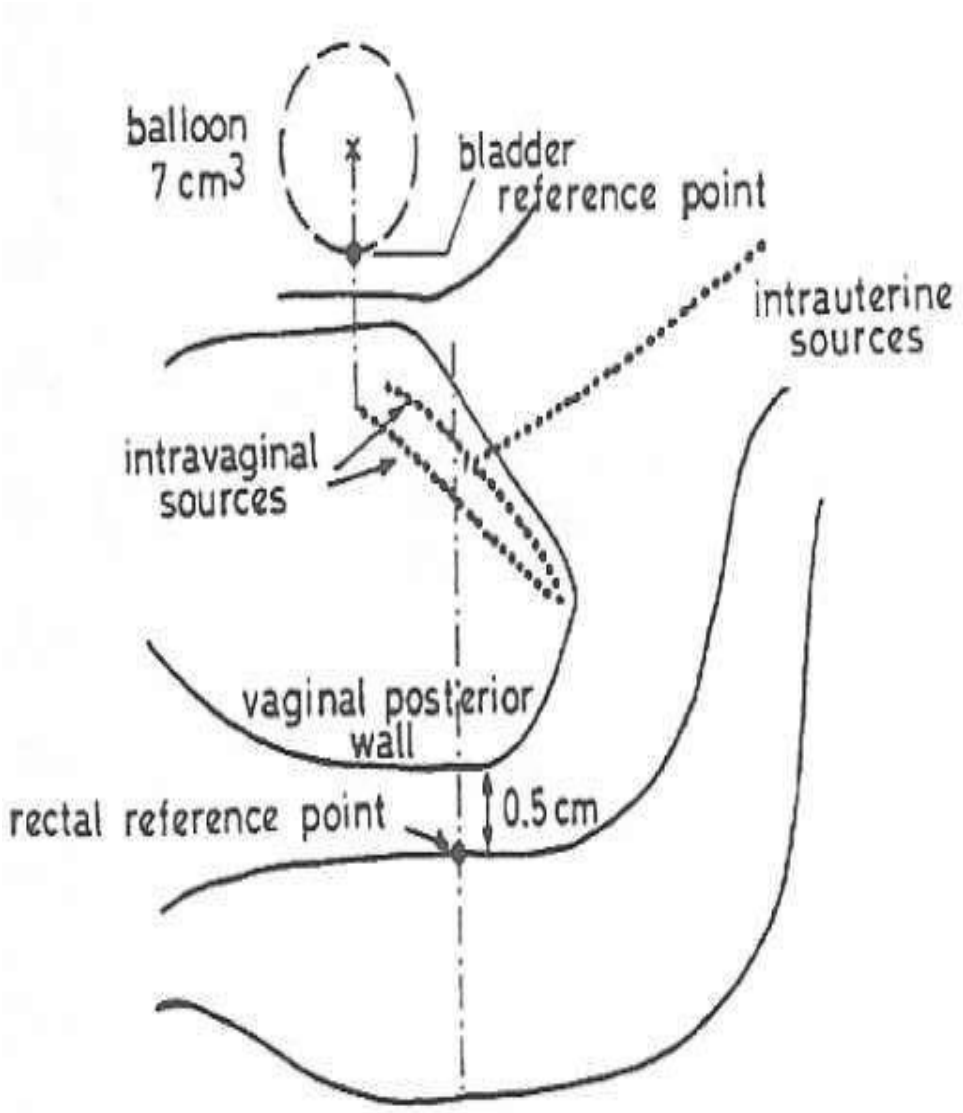
- ICRU recommends:
  - Foley balloon filled with 7cc of radiopaque fluid and pulled down against urethra
  - On lateral radiograph reporting dose at a point at posterior surface of Foley balloon on AP line through centre of balloon.
  - On AP radiograph, reference point is taken at the centre of the balloon





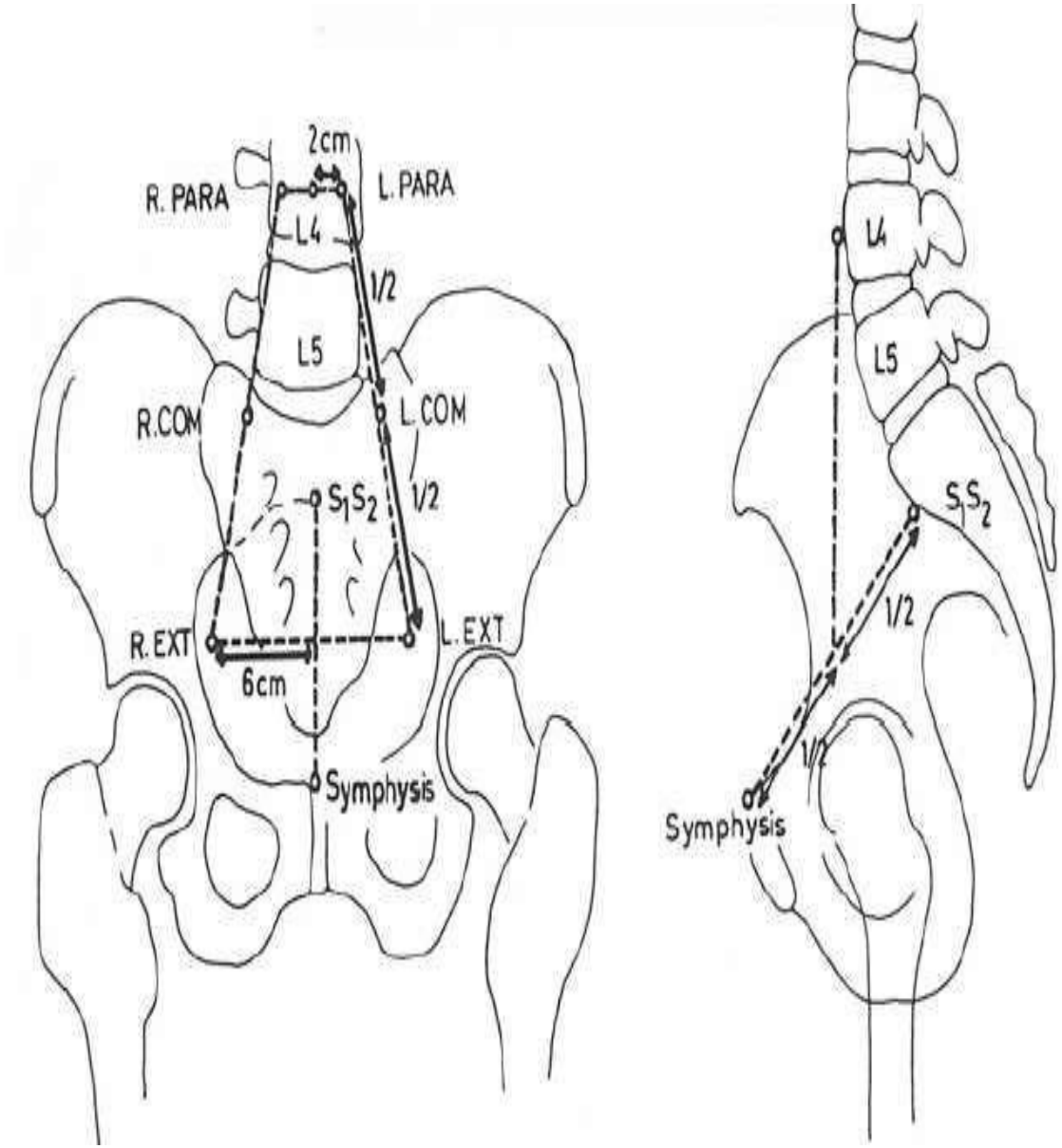
RECTAL POINT

- ICRU recommends:
  - The dose is calculated at a point 5 mm posterior to (opacified) vaginal cavity along an AP line midway between vaginal sources.
  - On the frontal radiograph, this reference point is taken at the intersection of (the lower end of) the intrauterine source through the plane of the vaginal sources



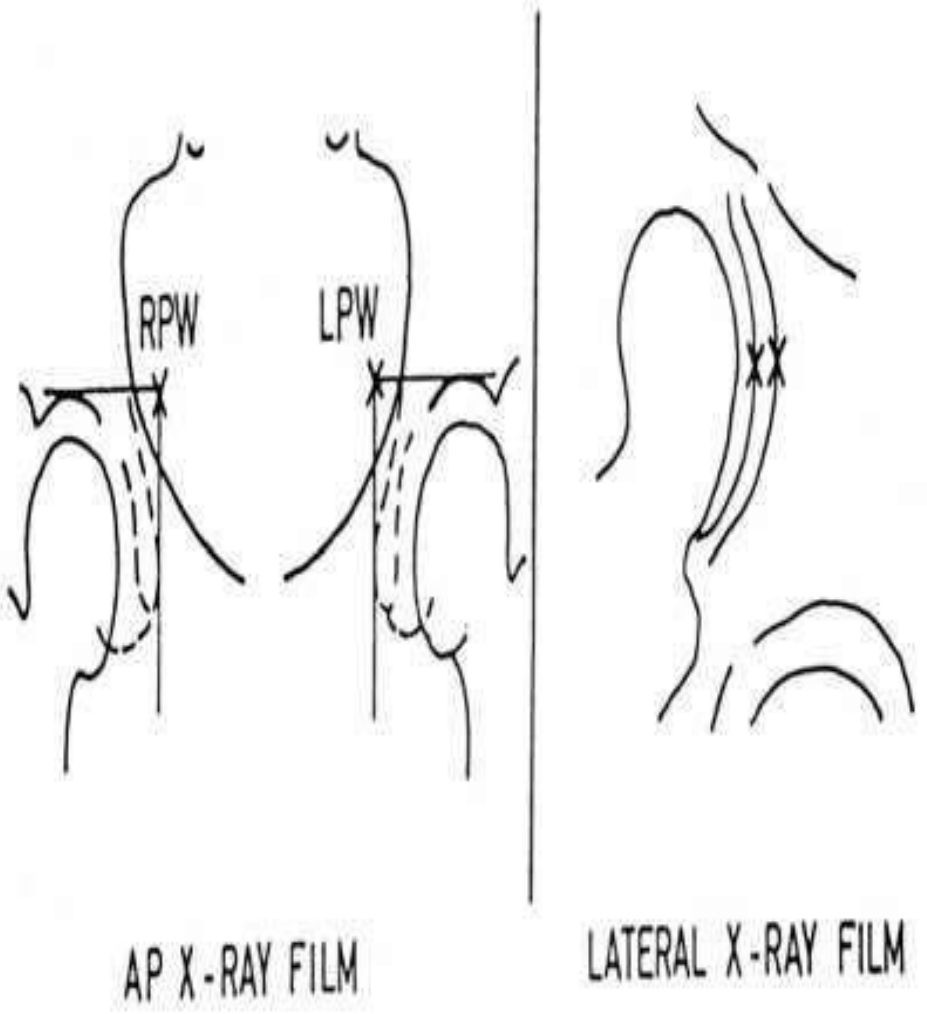
LYMPHATIC TRAPIZOID

- Lymphatic trapezoid represents dose at lower Para-aortic, common and external iliac L.N.
- A line is drawn from S1-S2 junction to top of symphysis, then a line is drawn from middle of this line to middle of ant. aspect of L4.
- A trapezoid is constructed in a plane passing through transverse line in pelvic brim plane and midpoint of ant. aspect of body of L4.



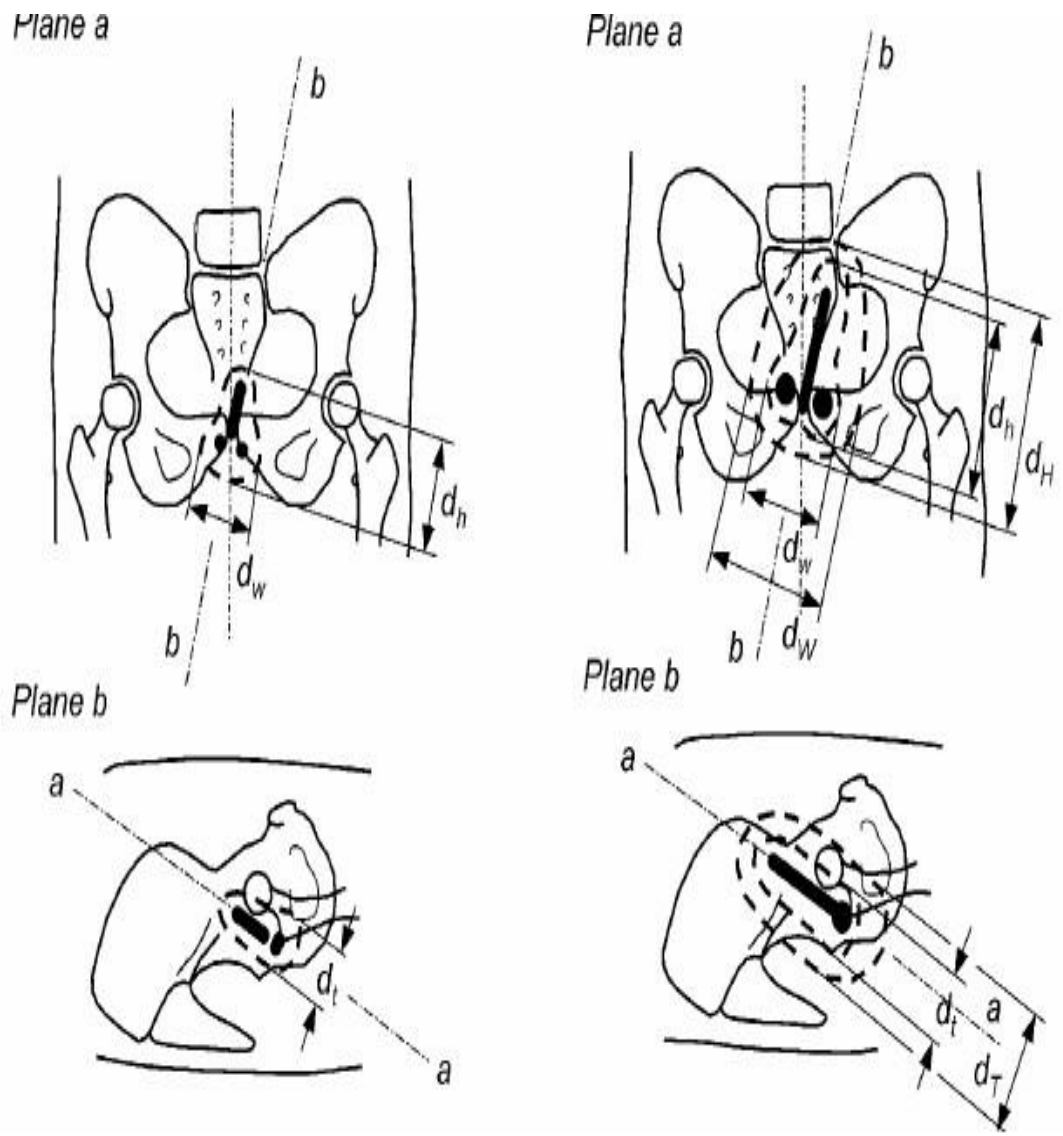
PELVIC WALL REFERENCE POINTS

- The pelvic wall reference point, represents absorbed dose at the distal part of the parametrium and at the obturator L.N.
- On anAP radiograph, pelvic-wall reference point is located at intersection of following lines
  - A horizontal line tangential to the highest point of the acetabulum,
  - A vertical line tangential to the inner aspect of the acetabulum.
- On a lateral radiograph, the highest points of the right & left acetabulum, in craniocaudal direction, are joined & lateral projection of the pelvic-wall reference point is located mid-way b/w these points.



Description of Reference volume

- Volume encompassed by the reference isodose, selected and specified to compare treatments performed in different centres using different techniques.
- ICRU (43) recommends reference volume be taken the as the 60-Gy isodose surface, resulting from the addition of dose contributions from any external-beam whole-pelvis irradiation and all I/C insertions.
  - Height ‘h’
  - Width ‘w’
  - Thickness ‘t’.
  - and *their product* should be reported separately



- Treated Volume
  - The Treated Volume is the pear and banana shape volume that received (at least) the dose selected and specified by the radiation oncologist to achieve the purpose of the treatment e.g., tumour eradication or palliation, within the limits of acceptable complications.
- Irradiated Volume
  - The irradiated volume is the volume, surrounding the treated volume, encompassed by a lower isodose to be specified, e.g., 90 – 50% of the dose defining the treated volume.
  - Reporting irradiated volumes is useful for interpretation of side effects outside the treated volume and for purpose of comparison

HIGH DOSE RATE

- After loading systems.
  - Developed in 1968 by Joslin
  - Initially Cobalt 60, now iridium 192.
- BED calculation of equivalence
  - Based on LQ model

For HDR: $\mathrm{BED} = Nd\left(1 + \frac{d}{\alpha/\beta}\right)$

For LDR: $\mathrm{BED} = NRt\left[1 + \frac{2R}{\mu(\alpha/\beta)}\left\{1 - \frac{1 - e^{-\mu t}}{\mu t}\right\}\right]$

- For equivalence to LDR the dose/# needs to be ~3 Gy.
- However, this based on the t1/2 of late reacting tissues – 1.5 hrs.
- If assumed to be 4 hrs., then dose/# be 6-12 Gy and HDR may be radio biologically better.
- Also, better geometrical sparing due to better packing away of critical organs

Advantages of HDR

1. Shorter treatment times, resulting in:
   - Less patient discomfort since prolonged bed rest is eliminated .
   - Reduced applicator movement during therapy.
   - Greater displacement of nearby normal tissues.
   - Possibility of treating larger number of patients.
2. Allows use of smaller diameter sources than are used in HDR:
   - Reducing the need for heavy sedation or general anesthesia (allowing treatment for high-risk patients who are unable to tolerate general anesthesia).
   - Making insertion of the tandem into the cervix easier.
3. Tailor dose distribution to target through optimization.
4. Elimination of exposure to personnel.

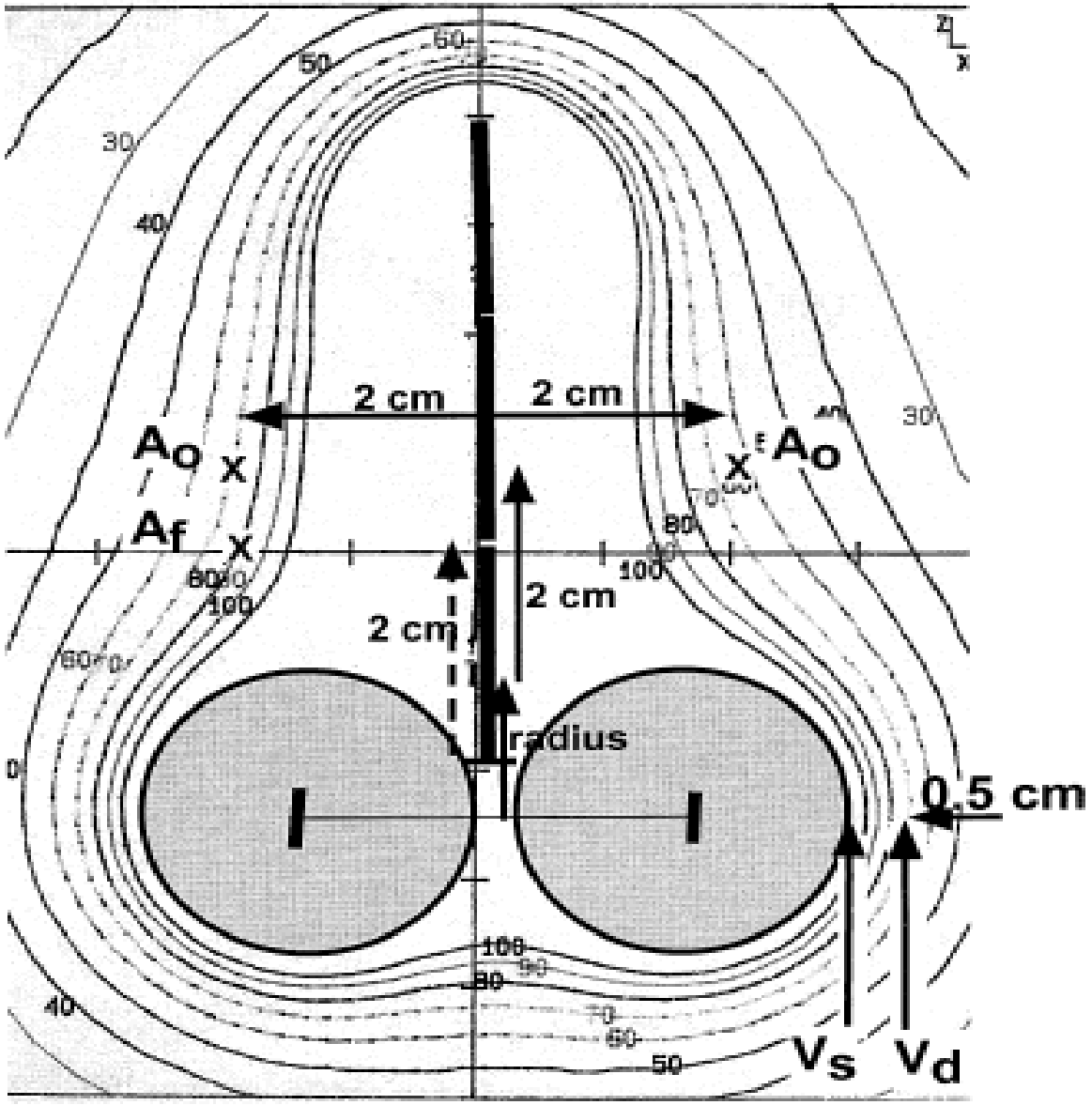
Disadvantages of HDR

1. Labor intensive (requires large staff during procedure)
2. Decreased therapeutic ratio (radio biologically, normal tissue becomes relatively more sensitive than tumor)
3. Increased probability of executing an error
4. Must know target and desired doses
5. Repeated multiple times – different geometry each time.

ABS RECOMMENDATIONS

ABS recommendation for locating point A

- From the point of intersection of the line connecting middle of both the ovoids with the central tandem, move superiorly along the tandem, 2cm + radius of the colpostats & then 2cm perpendicular to the tandem in the lateral direction.
- Dose reporting
  - Lateral vaginal surface V_s
  - 0.5 cm deep to vaginal surface V_d
  - Limit Vs dose to <150% of point A dose.
  - Nominal bladder point-ICRU 38
  - Nominal rectal point – ICRU 38
  - Keep bladder dose < 80Gy*
  - Rectal dose < 75 Gy*
  - Pelvic wall point – ICRU 38



ABS recommendation for LDR

- Procedure under analgesia/ anesthesia
- Use of 2 LDR applications in larger tumors (single if unreliable patient, excellent geometry, small tumor)
- Entire Rx completed in 8 wks.
- Place radio-opaque markers on cervix to determine relation of vaginal applicators to cervix.
- Use largest colpostat accommodated.
- Ideally – tandem bisects the colpostat on lateral view & tandem falls midway b/w colpostats & parallel to body axis on AP view.
- 7cc – foley’s bulb

Suggested doses for LDR brachytherapy

Table 2. Carcinoma of the uterine cervix: Suggested doses of external beam irradiation and LDR intracavitary brachytherapy*

		External irradiation (Gy)			LDR brachytherapy (Gy)	
Tumor stage	Tumor extent	Whole pelvis	Pelvic wall	Parametrial boost (Gy)	Dose to point A	Total dose to point A (Gy)
IA1		0	0	0	50–60	50–60
IA2	Superficial ulceration less than 1					
Selected IB1	cm in diameter or involving					
	fewer than two quadrants	0	0	0	60–70	60–70
IB1		19.8 or 45	50.4 or 45	0	55 or 30–35	75 or 75–80
IB2, IIA,†		45	45	0	40	85
IIB†		45	45	9–15	40	85
III†		45–50	45–50	9–15	40	85–90
IIB, IIIB, IV	Poor pelvic anatomy, patient not readily treated with intracavitary insertions (barrel-shaped cervix not regressing, inability to locate external os)	50	50	9–15	40	90
	Or interstitial	39.6–45	39.6–45	0–15	35–40*‡	75–85*‡

ABS recommendation for HDR

- Keep total duration less than 8 weeks
  - Interdigitate HDR with EBRT
  - Started 2 weeks after EBRT – weekly
  - If large tumor, start later – twice weekly.
  - Keep HDR dose < 7.5 Gy

EBRT (Gy) @ 1.8 Gy/fraction	No. of HDR fractions	HDR dose/ fraction
20	6	7.5
20	7	6.5
20	8	6.0
45	5	6.0
45	6	5.3

Early cervical Ca

EBRT (Gy) @ 1.8 Gy/fraction	No. of HDR fractions	HDR dose/ fraction
45	5	6.5
45	6	5.8
50.4	4	7.0
50.4	5	6.0
50.4	6	5.3

Advanced Ca

Results of Rx-cervix limited disease

Authors	N° pts	Stage	5-yr survival (%)	Local control (%)
Manchester 80-88 LDR	294	I/IIA	90-94 (DFS)	
Hunter 1993	45	IB	71 (OS)	
1993 (62)	70	IIB	52 (OS)	
Perez (87) LDR	384	IB	85	90
	128	IIA	70	81
	353	IIB	72	77
Fletcher (35) LDR	494	IB IIA MDAH	84	93
	207	IIB MDAH	70	82
French cooperative group	229	I MDAH	89 (89)	93 (95)
LDR	315	IIA MDAH	81 (85)	83 (88)
Horiot (53)	314	IIB MDAH	76 (76)	80 (78)
Kim (66) LDR	169	IB	82	89
	83	IIA	78	91
Lowrey (74 LDR	130	IB	81	88
	64	IIA	74	84
Pernot (92) LDR	173	IIA-B prox.	74	79
Coia (18)	203	IB	80	90
Joslin (64, 65) HDR	95	I	94	97
	170	II	62	74
Petereit (93) HDR	59	IB	86	85
	64	II	65	80
Vienna HDR	42	IB/IIA	85 (DSS)	97
Pötter (96)	124	IIB	69 (DSS)	82

Cervix extended disease

Authors	N° pts	Stage	5-yr survival (%)	5-y Local control (%)
Manchester 1993 LDR Hunter 2001 (62)	50	III	34 OS	
Perez (86) LDR	293 20	III IV	52 DFS 0	59 25
Houston MDAH (26, 28) Fletcher LDR (73)	73 a* 25 b* 983	IB_2 IIB (bulk) IIIB (UICC)	44 OS 60 OS 36 DSS	67 84 78
French cooperative group LDR (53)	266 216 32	IIIA MDAH IIIB MDAH IV	61 OS (62) 39 OS (50) 20 OS	68 (63) 45 (57) 18
Paris IGR (42) LDR	58 416	Distal II IIIA-B, IV	65 OS 42 OS	78 66
Pernot (92) LDR	60 107	Distal IIB III	70 OS 42 OS	77 54
Joslin (64, 65) HDR	106	III	38 OS	56
Petereit (93) HDR	50	IIIB	33 OS	44
Vienna HDR Pötter (96)	78 12	IIIB IVA	48 DSS 19 DSS	65 48

THANK YOU